wherein each of adjacent pairs of R^1 and R^2, R^3 and R^4 , and R^5 and R^6 are independently

(a) two adjacent hydrogen atoms, where R^2 may be an alkyl group, or

(b) form a bond so that the carbon atoms to which they are attached have a double bond therebetween;

R^7 is a hydrogen atom, a hydroxy group, a protected hydroxyl group, or an alkoxy group, or an oxo group together with R^1;

R^8 and R^9 are independently a hydrogen atom or a hydroxy group;

R^{10} is a hydrogen atom, an alkyl group, an alkyl group substituted by one or more hydroxy groups, an alkenyl group, an alkenyl group substituted by one or more hydroxy groups, or an alkyl group substituted by an oxo group;

X is an oxo group, a hydrogen atom and a hydroxy group, a hydrogen atom and a hydrogen atom, or a group represented by the formula $-CH_2O-$;

Y is an oxo group, a hydrogen atom and a hydroxy group, a hydrogen atom and a hydrogen atom, or a group represented by the formula $N\text{-}NR^{11}R^{12}$ or $N\text{-}OR^{13}$;

R^{11} and R^{12} are independently a hydrogen atom, an alkyl group, an aryl group or a tosyl group;

R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{22} and R^{23} are independently a hydrogen atom or an alkyl group;

R^{24} is an optionally substituted ring system that may contain one or more heteroatoms;

n is an integer of 1 or 2; and

wherein Y, R^{10} and R^{23}, together with the carbon atoms to which they are attached, may represent a saturated or unsaturated 5- or 6-membered nitrogen, sulfur and/or oxygen containing heterocyclic ring optionally substituted by one or more groups selected from the group consisting of an alkyl, a hydroxy, an alkoxy, a benzyl, a group of the formula $-CH_2Se(C_6H_5)$, and an alkyl substituted by one or more hydroxy groups, or a pharmaceutically acceptable salt thereof.

13. (New) The method of Claim 12, wherein said macrolides are admixed with one or more carriers or excipients.

14. (New) The method of Claim 12, wherein R^{24} is a cyclo(C_{5-7})alkyl group.

15. (New) The method of Claim 14, wherein said cyclo(C_{5-7})alkyl group is selected from the group consisting of

a) a 3,4-di-oxo-cyclohexyl group;

b) a 3-R^{20}-4-R^{21}-cyclohexyl group,

wherein R^{20} is a hydroxy, an alkyoxy group, an oxo group, or a $-OCH_2OCH_2CH_2OCH_3$ group, and R^{21} is a hydroxy, -OCN, an alkoxy group, a heteroaryloxy which may be substituted by a suitable substituent, a $-OCH_2OCH_2CH_2OCH_3$ group, a protected hydroxyl group, chloro, bromo, iodo, aminooxyalyloxy, an azido group, p-tolyloxythiocarbonyloxy, or $R^{25}R^{26}CHCOO-$, wherein R^{25} is a hydroxy, a protected hydroxy, an amino, a protected amino, and R^{26} is hydrogen or methyl, or R^{20} and R^{21} together form an oxygen atom in an epoxide ring; and

c) cyclopentyl group substituted by methoxymethyl, hydroxymethyl, protected hydroxymethyl, acyloxymethyl, a acyloxymethyl in which the acyl moiety contains a dimethylamino group which may be quaternized, or a carboxy group which may be esterified, an amino group, a protected amino group, a hydroxy group, a protected hydroxy group, and a aminooxyalyloxymethyl.

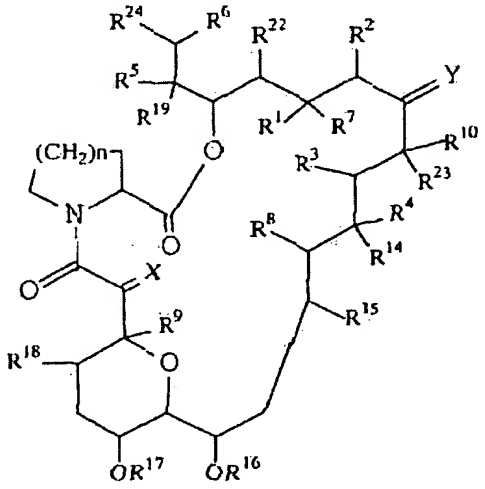
B1

16. (New) The method of Claim 12, wherein said macrolide of formula (I) is selected from the group consisting of tacrolimus, ascomycin, and 33-epi-chloro-33-desoxyascomycin.

17. (New) The method of Claim 12, wherein said pharmaceutically acceptable salt thereof is selected from an alkali metal salt, an alkali earth metal salt, an ammonium salt, an amine salt, a hydrate, and an ethanolate.

18. (New) The method of Claim 12, wherein said effective concentration is 0.0001 to 1000 mg per day.

19. (New) A method of treating a matrix metalloprotease-mediated disease comprising administering to a patient in need thereof an effective amount of one or more macrolides of the following formula (I):



(I)

wherein each of adjacent pairs of R^1 and R^2, R^3 and R^4 , and R^5 and R^6 are independently

(a) two adjacent hydrogen atoms, where R^2 may be an alkyl group, or

(b) form a bond so that the carbon atoms to which they are attached have a double bond therebetween;

R^7 is a hydrogen atom, a hydroxy group, a protected hydroxyl group, or an alkoxy group, or an oxo group together with R^1;

R^8 and R^9 are independently a hydrogen atom or a hydroxy group;

R^{10} is a hydrogen atom, an alkyl group, an alkyl group substituted by one or more hydroxy groups, an alkenyl group, an alkenyl group substituted by one or more hydroxy groups, or an alkyl group substituted by an oxo group;

X is an oxo group, a hydrogen atom and a hydroxy group, a hydrogen atom and a hydrogen atom, or a group represented by the formula $-CH_2O-$;

Y is an oxo group, a hydrogen atom and a hydroxy group, a hydrogen atom and a hydrogen atom, or a group represented by the formula $N\text{-}NR^{11}R^{12}$ or $N\text{-}OR^{13}$;

R^{11} and R^{12} are independently a hydrogen atom, an alkyl group, an aryl group or a tosyl group;

R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{22} and R^{23} are independently a hydrogen atom or an alkyl group;

R^{24} is an optionally substituted ring system that may contain one or more heteroatoms;

n is an integer of 1 or 2; and

wherein Y, R^{10} and R^{23}, together with the carbon atoms to which they are attached, may represent a saturated or unsaturated 5- or 6-membered nitrogen, sulfur and/or oxygen containing heterocyclic ring optionally substituted by one or more groups selected from the group consisting of an alkyl, a hydroxy, an alkoxy, a benzyl, a group of the formula $-CH_2Se(C_6H_5)$, and an alkyl substituted by one or more hydroxy groups, or a pharmaceutically acceptable salt thereof.

20. (New) The method of Claim 19, wherein said macrolides are admixed with one or more carriers or excipients.

21. (New) The method of Claim 19, wherein R^{24} is a cyclo(C_{5-7})alkyl group.

22. (New) The method of Claim 21, wherein said cyclo(C_{5-7})alkyl group is selected from the group consisting of

a) a 3,4-di-oxo-cyclohexyl group;

b) a 3-R^{20}-4-R^{21}-cyclohexyl group,

wherein R^{20} is a hydroxy, an alkyoxy group, an oxo group, or a $-OCH_2OCH_2CH_2OCH_3$ group, and R^{21} is a hydroxy, -OCN, an alkoxy group, a heteroaryloxy which may be substituted by a suitable substituent, a $-OCH_2OCH_2CH_2OCH_3$ group, a protected hydroxyl group, chloro, bromo, iodo, aminooxyalyloxy, an azido group, p-tolyloxythiocarbonyloxy, or $R^{25}R^{26}CHCOO$-, wherein R^{25} is a hydroxy, a protected hydroxy, an amino, a protected amino, and R^{26} is hydrogen or methyl, or R^{20} and R^{21} together form an oxygen atom in an epoxide ring; and

c) cyclopentyl group substituted by methoxymethyl, hydroxymethyl, protected hydroxymethyl, acyloxymethyl, a acyloxymethyl in which the acyl moiety contains a dimethylamino group which may be quaternized, or a carboxy group which may be esterified, an amino group, a protected amino group, a hydroxy group, a protected hydroxy group, and a aminooxyalyloxymethyl.

23. (New) The method of Claim 19, wherein said macrolide of formula (I) is selected from the group consisting of tacrolimus, ascomycin, and 33-epi-chloro-33-desoxyascomycin.

B1

24. (New) The method of Claim 19, wherein said pharmaceutically acceptable salt thereof is selected from an alkali metal salt, an alkali earth metal salt, an ammonium salt, an amine salt, a hydrate, and an ethanolate.

25. (New) The method of Claim 19, wherein said effective amount is 0.0001 to 1000 mg per day.

26. (New) The method of Claim 19, wherein said effective amount is 0.1 to 0.3 mg per kg per day.

27. (New) The method of Claim 19, wherein said matrix metalloprotease-mediated disease is one or more diseases selected from the group consisting of cartilage degradation, connective tissue degradation, rheumatoid arthritis, cerebral disease, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, tumor growth, tumor metastasis, tumor invasion, HIV-infection, decubitus, decubitus ulcer, restenosis, epidermolysis bullosa, sepsis, septic shock, neoplasm, psoriasis, neovascularization, multiple sclerosis.

28. (New) The method of Claim 27, wherein said matrix metalloprotease-mediated disease is selected from the group consisting of cartilage degradation, connective tissue degradation, and rheumatoid arthritis.

29. (New) The method of Claim 19, wherein said patient in need thereof is a mammal.